ADDRESS: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/488,164	06/07/95	KOPCHICK J	7707-015

EXAMINER

HM11/0410

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ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 04/10/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ ~~Responsive~~ to communication(s) filed on 22 January 1998

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 10-44, 46-64 is/are pending in the application.
Of the above, claim(s) 45 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 10-44, 46-64 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.

Transitional After Final Practice

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 22 January 1998 has been entered.

Response to Amendment

2. The claims 10, 29, 35, 40, 46-56, 61-62 have been amended and claims 63-64 have been added as requested in the amendment of paper # 14, filed 22 January 1998. Claims 10-64 are pending in the instant application. Claim 45 remains withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed 22 January 1998 have been fully considered but they are not deemed to be persuasive.

Information Disclosure Statement

6. The information disclosure statement filed 22 January 1998 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office on a PTO 1449. It has been placed in the application file (i.e. the references), but the information referred to therein has not been considered.

Specification

7. The abstract of the disclosure is objected to for the reasons of record. It is noted that Applicant submitted a new abstract. However, there was no amendment directing its entry into the instant specification. Correction is still required. See MPEP § 608.01(b).

8. Two amendments to the specification which were submitted in paper #14 could not be entered. The amendment at page 12, lines 11-12 could not be entered because "bGH ... A112D"

does not appear at this location. The amendment at page 13, lines 1-2 could not be entered because "serum glucose", "urea/nitrogen" and "triglyceride" does not appear at this location.

9. The amendment filed 22 January 1998 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: at page 7, line 31, "The growth-inhibitory hormone, or the gene encoding it, is useful in the production of small animals for use in research facilities where space is restricted, as pets for pet lovers with limited quarters, and as livestock for farmers having small tracts."

Applicant is required to cancel the new matter in the reply to this Office action.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 29-33 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record in paper #12.

It should be noted, that although claims were indicated as allowable in the previous Office action, new rejections appear in the instant Office action and no claim is currently found to be allowable. Therefore, any reference to allowable claims in Applicant's response as a basis for arguing allowable subject matter for the rejected claims is moot.

Applicant argues that the proper role of claim limitations is to define the metes and bounds of the invention and not to provide guidance to the person skilled in the art (see response at page 16). Where this may be true, the claims must contain sufficient structural elements in order to provide the claimed function in the case of product claims. Claims 29-33 do not provide sufficient structural elements to achieve the desired function of a growth hormone receptor antagonist (as pointed out in paper #12 at page 8). At page 9 of paper #12 it is noted that the other product claims contain further structural limitations which would be expected to provide the desired function (i.e. growth hormone receptor antagonist activity). The term "guidance" is used in the sense that these limitations provide structure to the polynucleotide which would serve to achieve the desired function.

Applicant argues that the Examiner has not established that disregarding the limitations set forth in claim 10 would result in a loss of GH receptor antagonist activity. The Examiner concedes that experimental data is not provided, however, rational scientific reasoning was provided in the previous Office action to support the assertion that one of ordinary skill in the art would not reasonably expect a protein which is only 50% identical to the native protein to be able to functionally bind a receptor or retain any biological activity. There is no art of record that supports the position that 50% of the GH molecule could be deleted and function as a receptor

antagonist. Furthermore, as stated at page 9 of paper #12, Gly 119 appears to be critical to receptor antagonist activity, and the instant claims do not require this element.

Applicant argues at pages 16-19 that the specification provides guidance which is not present in claim 10. However, claim 10 is not the subject of the instant rejection, therefore, these comments do not appear to bear on the issue at hand.

Applicant argues that the PTO has allowed patents which contain sequence identity language with a functional limitation (see pages 19-21 of the response). However, the issue at hand is not what has been allowed by the PTO in the past, but the applicability of the instant rejections to the claims of the instant application (see In re Hutchinson (CCPA) 69 USPQ 138).

At page 22, Applicant argues that "an activity limitation can be used to exclude what would otherwise be an inoperative embodiment and thereby save a claim to subject matter with 'established unpredictability'". This argument is not persuasive because, as stated previously, the claims must contain sufficient structural limitations to provide the recited activity. The recitation of 50% identity does not provide sufficient structural elements to afford the recited activity for the reasons given above, therefore the claims are not enabled. The claims in Mark et al. only contained mutations of the cysteine residues; the instant claims encompass deletion of as much as half of the protein and does not even include the presence Gly119, which appears to be a critical residue for the recited activity.

Applicant's arguments at page 22 (item 11) and continuing to page 25 are not persuasive. Applicant argues that the additional limitation in claim 64 limits the nature and site of the

mutations, but more broadly defines the reference hormone. This limitation has been deemed new matter (see rejections below), and therefore, is not enabled by the instant specification as filed.

12. Claims 46-60 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record in paper #12.

Applicant argues that dosage amounts, frequencies, routes of administration, and gene therapy is disclosed at page 37, lines 6-12; page 35 lines 2-9 and lines 31-34. However, as stated in Office action of paper #12 at page 12, "the instant specification fails to provide even a single example of dosage amounts, dosage frequencies, or routes of administration **of any DNA sequence** encompassed by Applicant's claimed invention for the alleviation of any disease condition which may be associated with excess growth hormone activity" (emphasis added). Applicant states that the DNA dose could be systematically determined. However, this would require undue experimentation for the reasons of record (see page 12 of paper #12).

Applicant asserts that the citation of the NIH report is used to show a lack of utility/operability (see arguments at pages 27-29). This is incorrect because a utility rejection does not appear in the Office action of paper #12. Because the asserted utility is believable, a utility rejection was not made. However, the instant specification fails to enable the claims, and therefore, an ENABLEMENT rejection was made (not a UTILITY rejection).

13. Claim 61 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a transgenic mouse, comprising administering a DNA molecule encoding the growth hormone receptor antagonist of claim 11 operatively linked to a promoter to a mouse, which has not completed its growth, wherein expression of said DNA molecule results in mice of smaller skeletal size, does not reasonably provide enablement for a method as described in claim 61. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record in paper #12.

Applicant did not provide any additional arguments regarding this claim, therefore, the rejection is maintained for the reasons of record.

14. Claims 10-44 and 46-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims now recite a proviso "that said polypeptide does not correspond to human growth hormone with all of the following substitutions and no others: Y111V, L113I, K115E, D116Q, E118K, E119R, G120L, Q122E, T123G, G126L, R127I and E129S". M.P.E.P. 2173.05(i) states "any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453

(Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement." There is no basis in the instant specification as filed for this limitation and is therefore, new matter and fails to comply with the written description requirement.

Applicant's statements regarding the proviso only address the issue of prior art, and not enablement or new matter. Therefore, since no art rejections are being applied, these statements require no response in this Office action.

Claim 64 is directed to a DNA encoding a polypeptide which is at least 50% identical with a reference hormone selected from the group consisting of growth hormones, prolactins, and placental lactogens. The instant specification does not contemplate DNA's encoding polypeptides which are at least 50% identical to a reference hormone wherein the hormone is prolactin or placental lactogen. In fact, the specification only contemplates using growth hormones as the reference hormones (see for example page 6, lines 33-35; page 13, lines 30-33; page 14, lines 10-13; page 17, lines 16-37; page 18 lines 1-12). Therefore, DNA's encoding polypeptides which are at least 50% identical to a reference hormone wherein the hormone is prolactin or placental lactogen is deemed new matter.

15. Claims 10-44 and 46-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims encompass a polynucleotide comprising a polynucleotide "encoding a growth hormone receptor antagonist which is a polypeptide which comprises an amino acid sequence which is at least 50% identical with the sequence of a first reference vertebrate growth hormone". However, the use of % identity is indefinite without a recitation of an algorithm for calculating this identity. In determining identity, there are a number of variables which must be selected and are necessary for the calculation of identity. Based on the selection of values for these variables, the % identity can vary immensely. For example, consider two sequences: acgtac and acac. These can be compared in any of four ways.

acgtac	4/6=67%	acgtac	2/6=33%
|| ||		||	
ac--ac	4/4=100%	acac	2/4=50%

Depending how gaps and lengths are calculated, the percent identity between these two simple sequences can vary from 100% to 33%. In addition, the reference George et al. is provided with this Office action which demonstrates the numerous types of algorithms which can be used to calculate identity and how selection of values for the variables will influence this calculation (i.e. gaps, lengths, etc.). Therefore, the recitation of %identity without the provision of a specific algorithm in the instant specification as how this identity is to be calculated is indefinite and the metes and bounds of the claims cannot be determined.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 8AM to 3PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Christine Saoud, Ph.D.
April 8, 1998
CS

JOHN ULM
PRIMARY EXAMINER
GROUP 1800